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EXAMINER

HOLLERAN, ANNE L

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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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*Ex parte* RANDALL W. NELSON, PETER WILLIAMS, and  
JENNIFER REEVE KRONE

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Appeal 2008-005047  
Application 09/024,988  
Technology Center 1600

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Decided:<sup>1</sup> May 29, 2009

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Before DEMETRA J. MILLS, RICHARD M. LEBOVITZ, and  
MELANIE L. McCOLLUM, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

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<sup>1</sup> The two-month time period for filing an appeal or commencing a civil action, as provided for in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

This is a decision on appeal from the Examiner's final rejection of claims 31, 33, 40, and 48-50. Jurisdiction for this appeal is under 35 U.S.C. § 6(b). We affirm.

#### STATEMENT OF THE CASE

The claims are to methods for quantifying an analyte in a specimen using matrix-assisted laser desorption/ionization (MALDI) mass spectroscopy. The method involves combining a specimen with an internal reference species ("IRS"), combining the IRS with an affinity reagent, and "analyzing and quantifying" the analyte in the specimen by MALDI using the detected signals of the analyte and IRS.

Claims 31, 33, 40, and 48-50 are appealed and stand rejected by the Examiner as follows:

1. Claims 31, 33, 40, and 48-50 under the judicially created doctrine of obvious-type double patenting as unpatentable over claims 31, 33, 37, 39, 44, and 46 of copending Application Serial No. 09/808,314, filed Mar. 14, 2001 (Ans. 5).

2. Claims 31, 33, 40, and 48-50 under 35 U.S.C. § 103(a) as obvious over Duncan<sup>2</sup> and Nuwaysir<sup>3</sup> (Ans. 7); and

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<sup>2</sup> Duncan et al., *Quantitative Analysis of Low Molecular Weight Compounds of Biological Interest by Matrix-assisted Laser Desorption Ionization*, 7 RAPID COMMUNICATIONS IN MASS SPECTROM. 1090-1094 (1993).

<sup>3</sup> Lydia M. Nuwaysir and John T. Stults, *Electrospray Ionization Mass Spectrometry of Phosphopeptides Isolated by On-Line Immobilized Metal-Ion Affinity Chromatography*, 4 J. AM. SOC. MASS SPECTROM 662-669 (1993).

3. Claims 31, 33, 40, and 48-50 under 35 U.S.C. § 103(a) as obvious over Duncan and Hutchens (U.S. Pat. 6,528,320, continuation of an application filed May 28, 1993) (Ans. 9).

Claims 31 is representative and reads as follows:

31. A method for quantifying an analyte in a specimen, said method comprising the steps of

a) combining said specimen with an internal references species (IRS) of known concentration, in order to calibrate all subsequent steps; whereby said combination is referred to as an IRS-containing specimen;

b) combining said IRS-containing specimen with an affinity reagent, capturing and isolating said analyte and said IRS, wherein said IRS is a modified analyte with shifted molecular weight which binds to said affinity reagent;

c) analyzing and quantifying said analyte wherein analyzing and quantifying comprises using matrix-assisted laser desorption/ionization (MALDI) to resolve distinct signals for said analyte and said IRS to determine the ratio of the analyte signal to the IRS signal.

#### THE AMENDMENT

Appellants filed a claim amendment date stamped Sep. 14, 2006 (the “Amendment”), prior to filing the appeal of the rejections in this application. Appellants acknowledge that the Examiner refused to enter the Amendment (App. Br. 2), but argue that the Examiner’s action was improper.

The Examiner did not act improperly. The Examiner’s refusal to enter the amendment was an “action . . . of”<sup>4</sup> the Examiner and therefore its

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<sup>4</sup> § 1.181 Petition to the Director.

“(a) Petition may be taken to the Director:

(1) From any action or requirement of any examiner in the ex parte prosecution of an application . . .”

propriety was petitionable under 37 C.F.R. § 1.181(a). The Board's jurisdiction is over decisions by a primary examiner to reject claims. 35 U.S.C. § 134(a). By statute, therefore, the Board's jurisdiction does not extend to the Examiner's action in refusing to enter an amendment. Accordingly, Appellants' argument (App. Br. 8-11) that the Examiner incorrectly refused to enter the Amendment have not been considered.

#### OBVIOUS-TYPE DOUBLE PATENTING REJECTION

Claims 31, 33, 40, and 48-50 stand provisionally rejected under the judicially created doctrine of obvious-type double patenting as unpatentable over claims 31, 33, 37, 39, 44, and 46 of copending Application Serial No. 09/808,314, filed Mar. 14, 2001 (Ans. 5).

Application Serial No. 09/808,314 was abandoned. *See* Office Communication mailed Aug. 13, 2008 in Application Serial No. 09/808,314. The rejection is therefore dismissed.

#### OBVIOUSNESS OVER DUNCAN AND NUWAYSIR OR HUTCHEN

##### Statement of the Issues

The main bases for error in the Examiner's rejection raised by Appellants' are as follows:

- the Examiner failed to establish that the cited prior art meets all the limitations of the claims; and
- the Examiner failed to provide a reason for combining the cited prior art to have made the claimed subject matter.

Findings of Fact (“FF”)

Duncan

1. Duncan describes experiments in which “[i]nternal standards were used to demonstrate that matrix-assisted laser desorption/ionization (MALDI) mass spectroscopy can be applied to the quantitative analysis of low molecular weight polar compounds” (Duncan, Abstract).
2. Duncan states that “a suitable internal standard . . . should mimic the behaviour of the analyte at all stages during sample preparation and analysis” (Duncan, 1090, col. 2). Duncan states that structural analogs, such as homologs and stable-isotope labeled compounds, have been used for this purpose (*id.*).
3. In Duncan’s examples, isotope analogs and a peptide structural analog were used as internal standards for quantifying the presence of corresponding unmodified analytes (Duncan, 1090-1091).
4. Duncan suggests that MALDI be coupled with immunoaffinity separation (Duncan, 1094).

Nuwaysir

5. Nuwaysir describes a method of using metal-ion affinity chromatography to purify samples containing phosphopeptides before they are analyzed by MALDI (Nuwaysir, 663, col. 1; 664, col. 2 under heading “IMAC” (immobilized metal-ion affinity chromatography); 665, col. 1) (Ans. 8-9).
6. The samples were applied to the IMAC column, phosphopeptide eluted, and then the phosphopeptide was subjected to mass spectroscopy (Nuwaysir, 664, col. 2 to 665, col. 2).

Hutchens

7. Hutchens describes a method of capturing an analyte from a sample on a probe tip derivatized with an affinity reagent that binds the analyte followed by mass spectroscopy (Hutchens, col. 3, ll. 38-50; col. 4, ll. 50-56; Ans. 11).
8. The affinity reagent can be a metal ion, a protein, a peptide, a nucleic acid, or a dye (Hutchens, col. 7, ll. 5-10; Ans. 11).

Claim 31

9. Claim 31 is to a method for quantifying an analytes in a specimen comprising three steps:
- a) combining the specimen with an internal reference species (IRS) to produce “an IRS-containing specimen”;
  - b) combining the IRS-containing specimen with an affinity reagent; and
  - c) analyzing and quantifying the analytes using MALDI “to resolve distinct signals for said analyte and said IRS to determine the ratio of the analyte signal to the IRS signal.”
10. The IRS is recited to be a “modified analyte.”
11. An “affinity reagent” is defined in the Specification to be “a type of antigen or antibody immobilized to a solid substrate” (Spec. 11) that “bind[s] with another molecule” (*id.*). The “another molecule” in this case would be the “analyte” or “IRS” of claim 31.
12. Claim 31 does not require the analyte or IRS to be released from the affinity reagent prior to quantifying by MALDI (*see* Ans. 12).
13. Appellants do not dispute:

14. • the Examiner's findings on pages 7-8 of the Answer that Duncan describes a method comprising steps a) and c) as recited in claim 31, but which lacks an exemplified step involving an affinity reagent as in step b) of the claim; and
15. • the Examiner's findings that each of Nuwaysir and Hutchens describe utilizing an affinity step as in step b) of claim 31 (Ans. 8-9 & 11).

### Analysis

#### Duncan and Nuwaysir

In challenging the Examiner's rejection of claim 31 over Duncan and Nuwaysir, Appellants contend that they have amended the claims by

further limiting the claim language to show that quantification of the analyte is done by capturing the analyte and an internal reference species (IRS) with an affinity reagent, releasing the analyte and IRS from the affinity reagent, and then analyzing and quantifying the analyte using matrix-assisted laser desorption/ionization (MALDI) on the released analyte and IRS.

(App.Br. 14.)

The Examiner did not enter the Amendment limiting the claim language in the manner described by Appellants (*see supra* at p. 3). Appellants acknowledge that the claim Amendment was not entered (App. Br. 2), but still argue the rejection on the merits of the unentered Amendment (*id.* at 14 as quoted above). As the Amendment was not entered by the Examiner, it is not considered to be part of the appealed claims. The arguments relating to the non-entered Amendment are therefore not persuasive because they address limitations not recited in the claim.



Appellants contend that claim 31 is distinguished over Nuwaysir because the amended claim excludes additional clean-up or purification steps which are stated to be disclosed in Nuwaysir (App. Br. 14).

The Amendment was not entered (App. Br. 2). Appellants do not contend that unamended claim 31, as it appears in this appeal, excludes such steps nor do we interpret the claim so narrowly.

Appellants also contend that the Examiner has not provided “any express or implied suggestion” to combine the teachings in Duncan and Nuwaysir (App. Br. 16).

To the contrary, Duncan explicitly suggests utilizing immunoaffinity separation in combination with MALDI (FF4; Ans. 7) as in claim 31. The Examiner reasoned that persons of ordinary skill in the art would have combined Duncan with Nuwaysir “in the contemplation of the necessity of a clean-up step”<sup>5</sup> as suggested by Duncan (Ans. 9; FF4). Therefore, the Examiner provided an explicit fact-based reason for reaching the conclusion that the claimed subject matter would have been obvious to a person of ordinary skill in the art.

For the foregoing reasons and those set forth in the Answer, we affirm the rejection of claim 31 over Duncan and Nuwaysir. Claims 33, 40, and 48-50 fall with claim 31 because separate reasons for their patentability were not provided. *See* 37 C.F.R. § 41.37(c)(1)(vii).

Duncan and Hutchens

Appellants contend that Hutchens performs mass spectroscopy with the analyte *and* affinity reagent on the probe in contrast to the claims which

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<sup>5</sup> A clean-up step is understood to mean immunoaffinity separation (FF4).

are directed to, inter alia, “releasing the isolated analyte species and IRS from the affinity reagent, and then detecting” it using mass spectroscopy (App. Br. 15).

Claim 31 does not require the analyte and IRS to be released from the affinity reagent prior to analysis by MALDI (FF12). Step b) of claim 31 recites that the IRS is combined with the affinity reagent and step c) is to “analyzing and quantifying” the analyte by resolving “signals for” the analyte and IRS. We discern no claim language that would require the analyte or IRS to be released prior to MALDI analysis in step c). To the extent that such language appears in the Amendment of Sep. 14, 2006 (*see* above), we reiterate that the Amendment was not entered and is therefore not a part of the appealed claims.

Appellants also contend that the Examiner has not provided “any express or implied suggestion” to combine the teachings in Duncan and Hutchens (App. Br. 16).

To the contrary, Duncan explicitly suggests utilizing immunoaffinity separation in combination with MALDI (FF4; Ans. 10-11) as in claim 31. The Examiner reasoned that persons of ordinary skill in the art would have combined Duncan with Hutchens “in the contemplation of the necessity of a clean-up step” as suggested by Duncan (Ans. 11; FF4). Therefore, the Examiner provided an explicit reason for reaching the conclusion that the claimed subject matter would have been obvious to the ordinary skilled worker.

For the foregoing reasons and those set forth in the Answer, we affirm the rejection of claim 31 over Duncan and Hutchens. Claims 33, 40, and 48-

50 fall with claim 31 because separate reasons for their patentability were not provided. *See* 37 C.F.R. § 41.37(c)(1)(vii).

### CONCLUSIONS OF LAW

The Examiner established that the cited prior art meets all the limitations of the claims and provided a logical fact-based reason for combining the cited prior art to have made the claimed subject matter.

### SUMMARY

The obvious-type double-patenting rejection over Application Serial No. 09/808,314 is dismissed because the application was abandoned.

The rejection of claims 31, 33, 40, and 48-50 over Duncan and Nuwaysir is affirmed.

The rejection of claims 31, 33, 40, and 48-50 over Duncan and Hutchens is affirmed.

### TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

### AFFIRMED

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